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CONTENTS/SUMMARIES

Molecular and Cellular Regulation of Autotrophic Carbon Dioxide Fixation in Microorganisms. F. Robert Tabita..... 155–189

Summary: Many diverse bacteria depend on carbon dioxide as their sole source of carbon. These autotrophic organisms, for the most part, use the Calvin reductive pentose phosphate pathway to assimilate carbon dioxide, a process similar to the one that occurs in eucaryotic algae and higher plants. Facultatively autotrophic bacteria, capable of both lithoautotrophic and organoheterotrophic metabolism, are convenient systems to examine the molecular and cellular regulation of carbon dioxide fixation. Biochemical and molecular studies on these organisms showed that both transcription and posttranscription is controlled. With the cloning and expression in Escherichia coli of all the important structural genes of the Calvin cycle, particularly ribulose 1,5-bisphosphate carboxylase/oxygenase and phosphoribulokinase, site-directed mutagenesis studies have begun to provide a better understanding of how the structure of these proteins relates to their function.

Nitrate Respiration in Relation to Facultative Metabolism in Enterobacteria. Valley Stewart..... 190–232

Summary: Nitrate is the most efficient electron acceptor for anaerobic respiration in members of the Enterobacteriaceae. The metabolism of nitrate-respiring cells is in an intermediate state between "aerobiosis" and "anaerobiosis"; for example, the tricarboxylic acid cycle is incomplete, but other anaerobic respiratory and fermentation enzymes are not synthesized. The nitrate respiratory chain functions with electron donors such as formate, reduced nicotinamide adenine dinucleotide, and lactate and requires quinone and specific cytochromes b. The terminal enzyme, nitrate reductase, is a membrane-bound complex of at least three subunits. The active-site subunit (α) contains molybdenum cofactor and nonheme iron and faces the cytoplasm. The cytochrome b subunit (γ) faces the periplasm. Thus, it is hypothesized that a chemiosmotic gradient is formed by the release of two protons in the periplasm (concomitant with quinol oxidation) coupled to the consumption of two protons in the cytoplasm (concomitant with nitrate reduction). Chlorate-resistant mutants (chl) lack the activities of all molybdo-enzymes and are deficient in molybdenum cofactor synthesis or processing. The structural genes for nitrate reductase are organized in the nar operon. Nitrate reductase synthesis is induced by anaerobiosis, and anaerobically it is further induced by nitrate. Anaerobic induction requires the fnr gene product, which activates transcription of genes for anaerobic respiratory enzymes, but not of genes for other anaerobic enzymes. Nitrate induction requires the narL gene product, which activates transcription of the nar operon, and may repress transcription of genes for other anaerobic respiratory enzymes.

Continued on following page

Pilins of *Bacteroides nodosus*: Molecular Basis of Serotypic Variation and Relationships to Other Bacterial Pilins. T. C. Elleman...

233-247

Summary: Pili of Bacteroides nodosus, the causative organism of ovine footrot, are the major host-protective immunogen in current footrot vaccines. In vaccination trials, purified pili alone provide excellent protection against homologous serotypic challenge. Pilus-based protection is, however, confined within each serogroup, necessitating the inclusion of representatives from all major serogroups of B. nodosus in broad-spectrum vaccines. To define the sites and basis of antigenic variation in B. nodosus pilins and to determine the regions essential for the structural integrity, amino acid sequences of pilins from members of eight major serogroups of B. nodosus have been compared with each other and with pilins from other bacterial species. Pili of B. nodosus, Neisseria gonorrhoeae, Neisseria meningitidis, Moraxella bovis, Moraxella nonliquefaciens, and Pseudomonas aeruginosa share similar physical characteristics; their extensive amino acid sequence similarities indicate a homologous origin. A comparison of sequences permits the assignment of potential functions to different regions of the pilin molecule and indicates that pilins from B. nodosus can be classified into two distinct groups. Pilins from one group show no greater similarity to the other than do those from different bacterial species. The consequence of stringent functional conservation of pilin sequence for compatibility of pilus expression among bacterial species and the implication of this for pilus-based vaccines are considered.

Mechanisms of Gene Regulation in the General Control of Amino Acid Biosynthesis in *Saccharomyces cerevisiae*. Alan G. Hinnebusch

248-273

Summary: More than 30 unlinked genes encoding enzymes in amino acid biosynthetic pathways are coordinately regulated in Saccharomyces cerevisiae by a system known as general amino acid control. Transcription of all of these genes increases in response to starvation for any amino acid. Regulation by the general control system depends on a 9-base-pair nucleotide sequence, repeated in the 5'-noncoding deoxyribonucleic acid of each structural gene. This sequence is the binding site for the GCN4 protein, a positive regulator of transcription. GCN4 has separate regions for deoxyribonucleic acid binding and transcriptional activation that are strikingly similar to domains in other known regulatory proteins. GCN4 expression is regulated at the translational level by four AUG codons located in the leader of GCN4 messenger ribonucleic acid. The third and fourth AUG codons exert a nearly absolute block to translation of GCN4 protein-coding sequences in nonstarvation conditions. The first and second AUG codons function in starved cells to overcome translational repression. trans-Acting factors encoded by the GCD genes prevent the positive regulatory action of the first and second AUG codons. These factors are antagonized in starvation conditions by the products of three additional GCN genes, leading to increased synthesis of the GCN4 protein. One particular GCN factor, GCN3, has a direct role in negative regulation of the GCD1 and GCD12 gene products. Thus, general amino acid control is a multifaceted system that draws on several strategies of gene regulation to couple expression of amino acid biosynthetic enzymes to environmental changes.

Enzymes and Aflatoxin Biosynthesis. M. F. Dutton

274-295

Summary: Since their discovery in 1961, aflatoxins have been a source of continued interest to all of the life sciences, resulting in a vast literature. The reason for this curiosity and attendant research effort that far exceeds the importance and economic impact of these mycotoxins is not clear. That aflatoxin B₁, the major member of the group, is the most potent naturally occurring carcinogen known and is mutagenic and teratogenic, as well as an acute toxin, may be part of the answer. In addition to the morbid fascination that aflatoxin engenders, it presents a challenge to those who would unravel the metabolic pathway leading to its biosynthesis. Its biogenesis is not immediately apparent from its structure, which in itself is a chemical novelty. It is a polyketide, which has undergone a series of involved and spectacular modifications. By the use of specifically blocked mutants, labeled tracer experiments, and elegant nuclear magnetic resonance spectroscopic investigation, the major intermediates in the path-

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way were identified. Unfortunately, the application of powerful modern methodology has discouraged investigation of the enzymology of the steps leading to aflatoxin biosynthesis, which is unfortunate because knowledge about the enzymology of secondary metabolism is important for academic and practical reasons. This review brings together information on the enzymology of aflatoxin biosynthesis and points out the difficulties in studying fungal enzymology. Several hypothetical schemes are presented to stimulate further experimentation.

Defense Mechanisms Involving Fc-Dependent Functions of Immunoglobulin A and Their Subversion by Bacterial Immunoglobulin A Proteases. Mogens Kilian, Jiri Mestecky, and Michael W. Russell

296–303

Summary: The majority of immunoglobulin A (IgA) produced in the human body is secreted onto the vast area of mucosal surfaces, becoming the principal mediator of humoral immunity at these sites. The serum and mucosal IgA systems differ with regard to ontogeny, regulation, cellular origin, and molecular configuration of the respective immunoglobulin molecules. The functional properties of IgA from both systems depend on the Fc portion of the IgA molecule. Unlike IgG and IgM, which activate the complement and phagocytic systems, both serum and secretory IgA are relatively ineffective in interacting with these inflammatory effector systems. However, the polymeric configuration, ability to bind to a secretory component, hydrophilicity, and charge, conferred by the Fc part of secretory IgA, give this immunoglobulin isotype special mucosal defense properties. Serum IgA may have a unique function in regulating immune effector mechanisms mediated by the delivery of null or negative signals by its Fc region. Several microbial pathogens that colonize or invade through mucosal surfaces can interfere with such Fc-mediated functions of IgA by releasing proteases that specifically cleave the hinge region of human IgA subclass 1 (IgA1). These IgA1 proteases are virulence factors that enable mucosal pathogens to counteract secretory IgA-mediated defense mechanisms; they probably also affect the complex microbial ecology of mucosal surfaces, and they may cause temporary or local deficiencies in mucosal immunity. Furthermore, IgA1 proteases are hypothesized to provide a unique mechanism by which the three principal agents of bacterial meningitis can evade immune defense mechanisms and cause invasive disease.

ERRATUM

Homologous Recombination in Procaryotes. Gerald R. Smith.....

304